

REMARKS

Reconsideration and allowance are requested.

Claims 13-16, 21-23, 25-30, 35-37 and 41-46 are pending.

Non-elected claims 1 and 22-23 were withdrawn from consideration by the Examiner. Applicants cancel claim 1 without prejudice to future prosecution of that subject matter. But rejoinder of claims 22-23 is requested.

The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. Support for highly stringent conditions may be found, *inter alia*, at page 15, lines 25-27, of the specification.

It was alleged on page 2 of the Office Action that certified copies of the priority document were not received. Applicants provided the certified copies to the Receiving Office under PCT Rule 17. The attached Form PCT/IB/304 acknowledges receipt of the 12 priority documents. The International Bureau should have forwarded copies to each of the designated offices. See also M.P.E.P. § 1893.03(c). In accordance with M.P.E.P. § 1896 III, the Examiner is respectfully requested to consult with the Special Program Examiner to obtain the certified copies of the priority documents and to complete the file. Also see PCT Rule 17.2 stating, “No such Office shall ask the applicant himself to furnish it with a copy.”

The specification was objected to by the Examiner. The hyperlinks are rewritten so they are not browser-executable code.

Claims 13 and 15 were objected to under 37 CFR § 1.75(c) as allegedly being in improper form. They are amended in accordance with the Examiner’s suggestion.

Withdrawal of the objections is requested.

35 U.S.C. 112 – Enablement

The Patent Office has the initial burden to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04, and the cases cited therein. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with

the contested statement. *In re Marzocchi*, 169 USPQ 367, 370 (C.C.P.A. 1971). Specific technical reasons are always required. See M.P.E.P. § 2164.04.

Claims 13-16, 21 and 25-40 were rejected under Section 112, first paragraph, because it was alleged that the specification “does not reasonably provide enablement for any lipolytic enzyme or a protein with *no associated function* and having *varying sequence homologies* of 90% or 95% with respect to the to the sequences of SEQ ID NO: 34, 35 or 36 or a *function equivalent* of SEQ ID NO: 36 or a functional domain of lipolytic enzyme or a isolated lipolytic enzyme obtainable by expressing a polynucleotide which is hybridizable to the nucleotide sequence of SEQ ID NO: 34 or 35; or fusion proteins thereof.” Applicants traverse.

In their specification, Applicants disclose a total of **13** different lipolytic enzymes from *Aspergillus niger*. As shown in Table 1 (page 7 of Applicants' specification), the lipolytic enzyme of SEQ ID NO:36 corresponds to NBE045. Although NBE045 was not included in the different activity measurements described in Example 3 and summarized in Table 3 (page 51 of Applicants' specification) NBE045 was used in different baking experiments (see Examples 4 and 5) to demonstrate that it has lipase activity.

Applicants' disclosure, known lipolytic enzymes in the prior art, and the high level of skill permits the skilled artisan to modify the polypeptide of SEQ ID NO: 36, to make the fusion or recombinant enzymes, and to assay for their lipase activity and their ability to improve baking. To facilitate prosecution, the limitation “functional equivalent” is deleted because it is not required for patentability.

The technology used by skilled persons in this art are also described in Applicants' specification. These are routine and modifications would be guided by known chemistry (e.g., the properties of amino acids and their location in the enzyme) and comparison with the 12 other enzymes of the invention and those known in the prior art. The Examiner alleges that it is not routine in the art to screen for multiple modifications. Applicants disagree. Recombination and mutagenesis are routine in the art; products are also routinely screened for enzymatic activity. If this rejection is maintained, Applicants respectfully request that the Examiner provide evidence to support the allegation that screening is not routine in the art of protein engineering.

Now the four specific objections (A) to (D) on pages 4-5 of the Office Action are addressed:

(A) Whether the specification establishes regions of the protein structure which may be modified without affecting lipase enzyme activity. Note that multiple fungal lipolytic enzymes were disclosed in Applicants' specification and are known in the art. All of them were found to have similar molecular architecture with a central beta-sheet and a catalytic triad consisting of serine, histidine, and a carboxylate group reminiscent of serine proteases (see, for example, the introduction of Namboodiri). The amino acid sequences of the different lipases vary greatly (see also the 102 and 103 section). This shows that outside the catalytic center of the lipolytic enzyme, many modifications are permitted.

(B) Whether the specification establishes the general tolerance of lipase enzyme to modification and extent of such tolerance. As noted above, a large amount of substitution in the amino acid sequence is permitted while still retaining lipase activity.

(C) Whether the specification provides a rational and predictable scheme for modifying any lipase enzyme residues with an expectation of obtaining the desired enzymatic or biological function. Again, the comments under (A) establish modification is rational (e.g., protein engineering has been on a rational basis for a long time) and there is an expectation of retaining (or even improving) the properties of enzymes.

(D) Whether the specification provides sufficient guidance as to which of the essentially infinite possible choices is likely to be successful. By limiting the claims to at least 95% sequence identity and highly stringent hybridization, the choices confronted by the skilled artisan are greatly reduced.

As suggested by the Examiner, the reaction conditions for highly stringent hybridizing and washing are recited in claim 15.

Withdrawal of the enablement rejection made under Section 112, first paragraph, is requested because it would not require undue experimentation for a person of skill in the art to make and use the claimed invention.

35 U.S.C. 112 – Written Description

The specification must convey with reasonable clarity to persons skilled in the art that applicant was in possession of the claimed invention as of the filing date sought. See *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). But the Patent Office has the initial burden of presenting evidence or a reason why persons of ordinary skill in the art would not have recognized such a description of the claimed invention in the original disclosure. See *In re Gosteli*, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). A specification need not teach, and preferably omits, what is well known in the art. See *Hybritech v. Monoclonal Antibodies*, 231 USPQ 81, 94 (Fed. Cir. 1986).

Claims 13-16, 21 and 25-40 were rejected under Section 112, first paragraph, as allegedly “failing to comply with the written description requirement.” Applicants traverse because the specification teaches a representative number of species of the claimed genus. Their specification discloses 13 different lipolytic enzymes from *Aspergillus nige*. The genus is adequately described.

Withdrawal of the written description rejection made under Section 112, first paragraph, is requested because the specification conveys to a person skilled in the art that Applicants were in possession of the claimed invention as of the filing date.

35 U.S.C. 112 – Definiteness

Claims 13-14, 16, 21 and 25-40 were rejected under Section 112, second paragraph, as allegedly “indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” Applicants traverse because the limitations that the Examiner objected to are deleted or replaced.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 102 – Novelty and Nonobviousness

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical

invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See *id.* ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See *id.* at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning"). Thus, a *prima facie* case of obviousness requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn* at 1335; see *KSR* at 1396. An inquiry is required as to "whether the improvement is more than the predictable use of prior art elements according to their established functions." *Id.* at 1396. But a claim that is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* Finally, a determination of *prima facie* obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 13-14, 16, 28, 32, 36 and 39 were rejected under Section 102(a) as allegedly anticipated by or, in the alternative, under Section 103(a) as allegedly obvious over Namboodiri et al. (Lipids, vol. 35, no. 5, pp. 495-502, 2000) or Sugihara et al. (Agric. Biol. Chem., vol. 52, no. 6, pp. 1591-1592, 1988). Applicants traverse.

According to the Examiner, Namboodiri teaches a lipase with a molecular weight of about 35.5 kd from *Aspergillus niger* and Sugihara teaches a lipase with a molecular weight of about 35 kd from *Aspergillus niger*. But the Examiner's calculated molecular

weight for a polypeptide of SEQ ID NO: 36 is incorrect. Applicants calculated that their claimed polypeptide has a molecular weight of about 26.7 kd as shown in Table 2 (see page 50 of the specification). Applicants' calculation is confirmed independently by <http://www.innovagen.se/custom-peptide-synthesis/peptide-property-calculator/peptide-property-calculator.asp>. Therefore, the cited documents neither anticipate nor make obvious the polypeptide of Applicants' claimed invention.

Withdrawal of the Section 102 and Section 103 rejections is requested because the cited documents fail to disclose or make obvious limitations of the claimed invention.

Conclusion

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if additional information is required

Respectfully submitted,

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NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

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Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
19 Augu 2002 (19.08.02)	02102168.8	EP	10 Nove 2003 (10.11.03)
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19 Augu 2002 (19.08.02)	02102170.4	EP	10 Nove 2003 (10.11.03)
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